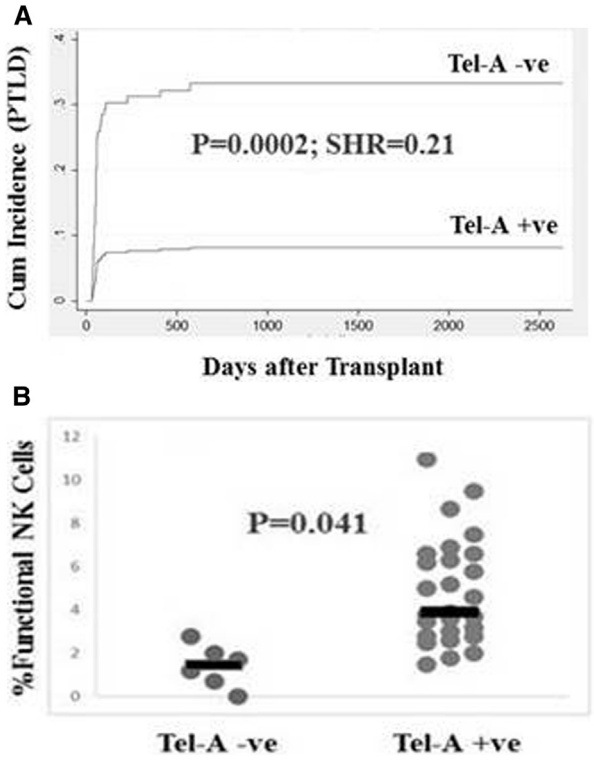

Figure 1. Influence of KIR Telomeric-A (Tel-A) motifs on [A] the development of PTLD after allogeneic HCT; and [B] NK cell response against EBV transformed cells.

Conclusions: NK cell responsiveness, a function of KIR gene repertoire has a profound effect on the development of PTLD. KIR genotype based identification of HCT donor-recipient pairs at high risk of developing PTLD will enable closer monitoring of EBV DNAemia and facilitate prompt therapy.

16

Outcomes of Second Unrelated Donor Cord Blood Transplants (UCBT) Performed in Children with Graft Failure of Autologous Recovery Following the First UCBT

Alicia McFarren [1], *P. Brian Smith* [2], *Kristin Page* [3], *Heather B. Allewelt* [4], *Suhag Parikh* [4], *Timothy A. Driscoll* [4], *Paul L. Martin* [4], *Joanne Kurtzberg* [4], *Vinod K. Prasad* [4].
[1] *Pediatric Hematology, Oncology and Blood & Marrow Transplantation, Children's Hospital of Los Angeles, Los Angeles, CA;* [2] *Division of Quantitative Sciences, Pediatrics, Duke University Medical Center, Durham, NC;* [3] *The Carolinas Cord Blood Bank and Robertson Cell and Translational Therapy Program, Duke University Medical Center, Durham, NC;* [4] *Pediatric BMT Program, Duke University Medical Center, Durham, NC*

Background: In the past 20 years, use of UCBT has improved access to transplantation, particularly in children and ethnic minorities. Rapid donor availability, partial HLA matching and low incidence of graft versus host disease (GVHD) are important advantages. UCBT outcomes have significantly improved in the last decade due to better graft availability and donor selection. However, a small fraction of recipients develop auto-recovery or graft failure and are candidates for a second transplant. In most cases, due to urgency and original limitations in donor choices, another cord blood unit (CBU) is the best option for these children.

Table
Characteristics of 2nd UCBT

Characteristics of 2nd UCBT		
Gender	**N**	**%**
Male	30	83.3
Primary Disease		
Heme malignancy	16	44.4
Inherited metabolic disease	10	27.8
Marrow failure	4	11.1
Immunodeficiency	3	8.3
Hemoglobinopathy	3	8.3
Reason for 2nd UCBT		
Primary graft failure	25	69.4
Late graft failure	3	8.33
Autologous recovery	8	22.2
Demographics	**median**	**range**
Age at 2nd UCBT (years)	7.4	1.5-20.9
Weight at 2nd UCBT (kg)	22.9	9.0-108.0
Time from 1st to 2nd UCBT (days)	61.5	42-3454
Cell Dose (n=39)		
Cryopreserved TNCs x 10^7/kg	5.6	1.3-21.9
Reinfused TNCs x 10^7/kg	4.6	1.1-18.1
Reinfused $CD34^+$ x 10^5/kg	1.4	0.1-15.0
Reinfused $CD3^+$ x 10^6/kg	9.1	1.5-34.4
Reinfused CFUs x 10^4/kg	5.7	0.0-175.4

Methods: Retrospective analysis of all pediatric patients (<21 years) undergoing UCBT at Duke between 1995 and 2013 who subsequently received a second UCBT due to graft failure or auto-recovery after the first UCBT (n=36) was conducted. Patients requiring second transplants for relapse were excluded. Kaplan-Meier estimates of overall survival (OS) and cumulative incidence (CI) of engraftment and GVHD were calculated. All received reduced intensity conditioning for the second transplant. The most common prep regimen was cyclophosphamide 60mg/kg x 2 and equine ATG 30mg/kg x 3 (n=15). Single cord (n=28), double cord (n=3) or cord +haplo graft (n=5) were the donor sources. Demographic, disease and graft characteristics are shown in the Table.

Results: The OS at 100 days, 1 year and 5 years was 50.0%, 37.1% and 33.3% respectively. Mortality was lower for patients transplanted after 2007, but the difference was not statistically significant (p=0.33) (see Figure). Median time to neutrophil (ANC 500) and platelet (50K) engraftments were 27 (range, 12-94) and 98 days (range, 37-434) respectively. The probability of neutrophil engraftment at day 42 was 64.3%. The CI of grades II-IV and grades III-IV acute GVHD, at 100 days was 47.1% and 31.3% respectively. Extensive/chronic GVHD was seen in 3 patients (CI=13.6%).

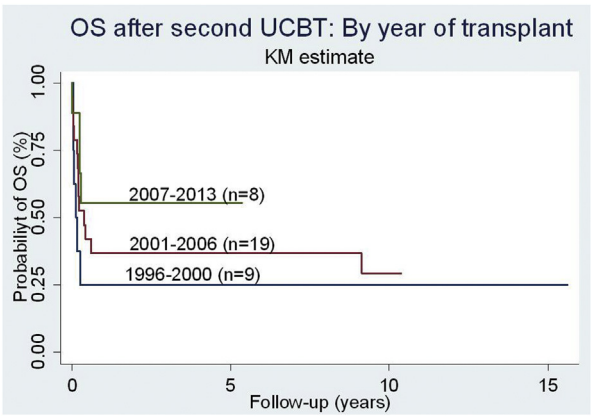

Figure.

Conclusions: Second UCBT resulted in acceptable survival particularly in the recent years when used as a rescue for failed initial UCBT. Use of a CBU allows quick second transplants and thus decreases the overall duration of cytopenias. Second UCBT should be offered as a viable option for children with a failed first UCBT.

17

Peripheral Blood Stem Cell Transplant in Aplastic Anemia

Pravas Chandra Mishra, *Tulika Seth, Manoranjan Mahapatra. Hematology, All India Institute of Medical Sciences, New Delhi, India*

Objective: We studied the outcome of heavily pre transfused aplastic anemia patients receiving peripheral blood stem cell transplant (PBSCT) from matched sibling donor.

Material: 72 consecutive blood/marrow stem cell transplants in 69 aplastic anemia patients over a period of 10 years in non HEPA filtered single rooms were recorded. Fludarabine 30 mg/m-2 D-10 to D-5, cyclophosphamide 60 mg/kg/day D-6 to D-5 and antithymocyte globulin 30 mg/kg/day D-4 to D-1 were used as conditioning regimen. Cyclosporine and methotrexate were used for graft versus host disease (GvHD) prophylaxis. ABO mismatched marrows underwent RBC depletion. No attempt to reduce antibody titres was done for ABO mismatched PBSCT.

Results: 63 patients underwent PBSCT; 2 underwent the procedure twice, 1 of whom had relapsed as acute myeloid leukemia. Of the 6 patients who received bone marrow stem cells, 2 relapsed and 1 underwent a successful PBSCT from the same donor. The median age of patients was 30 years (range 4-40 years); median time to transplant was 13.5 months (range 1-65 months); median transfusions before transplant were 22.5 (range 3-10). 28 (38.8%) patients had pre-existing infections at time of transplant. 65 patients received empirical antibiotics and 27 received empirical antifungals for febrile neutropenia during transplant. Positive blood culture for bacteria was recorded in 10 patients and a biopsy proven fungus (2 aspergillus, 2 mucor) in 4 patients; 5 other patients had possible fungal infection based on radiological features.

All patients and donors were CMV IgG positive at baseline. CMV reactivation was noted in 11 patients, 5 of whom were on steroids for GVHD; 3 patients subsequently suffered a graft failure.

55/72 (76%) patients are alive at median follow-up of 60 months ranging from 0-118 months. Acute GVHD was seen in 18/72 transplants (25%). 5 patients developed grade III-IV gut acute GvHD; 4 died. Chronic GvHD was seen in 32% of cases (20/62; 10 patients died before day 100). However these were mostly associated with dry skin and changes in pigmentation which generally subsided over time and well tolerated;1 patient had nephrotic syndrome at 3 years. Severe cGVHD as per NIH criteria was seen in only 5 patients. 17 patients had ABO major mismatch of which 5 patients developed PRCA. PRCA was managed with steroids and erythropoietin; the longest duration before recovery was 12 months. 17 patients died. Cause of early death (<day 100) were: acute GVHD 4, intracranial bleed 4, aspergillus 1, CMV 1, graft rejection 5 (more than 1 possible cause in some). Cause of death > day 100: chronic GVHD 1, graft rejection 2, tuberculosis 1.

Conclusions: PBSCT is safe in aplastic anemia patients whose transplant has been delayed and thereby heavily pre-transfused. The outcome and survival appear comparable to those achieved with historical bone marrow transplant data without apparent increase in morbidity on account of chronic GvHD.

18

Pre-Conditioning Steroids and Hydroxyurea Followed By Reduced Toxicity Conditioning (RTC) with ATG-Bu-FLU Is Safe and Effective in Allo-Sib-HSCT in Adolescents and Adults with Sickle Cell Anemia (SCA)

Said Yousuf Mohamed[1], *Hazzaa Alzahrani*[2], *Khaled T. Ibrahim*[3], *Ghada Elgohary*[4], *Ahmed Y. Gamal*[5], *Amr Hanbali*[6], *Marwan Shaheen*[6], *Walid K. Rasheed*[6], *Wahiba Chebbo*[6], *Osama Ali*[7], *Rehab Albloushi*[7], *Ahmad Alhuraiji*[7], *Naeem Chaudri*[7], *Syed O. Ahmed*[7],

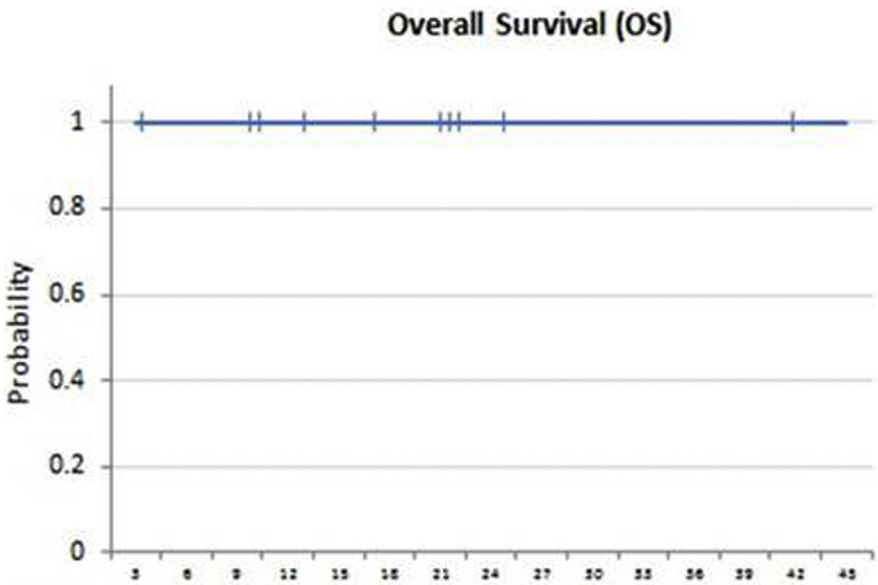

Figure 1a. Overall survival (OS) in months of 9 patients with SCA after Reduced Toxicity conditioning with ATG-BU-Flu and allo-sibling HSCT (median 22 mo; range 4-45 mo).